# FIG. 2A

Human G Protein Coupled Receptor Family

	THERAPEITTICS				Acuity, Alzheimer's	Diabetes, Cardiovascular	Cardiovascular, Respiratory Cardiovascular Parkingon's	Anti-inflammatory, Ulcers	Depression, Insomnia, Analgesic		Cardiovascular, Endocrine	Anti-inflammatory	Anti-inflammatory	Anti-inflammatory	Anti-inflammatory	Obesity			Carulovascular, Respiratory	Anti-intlammatory, Analgesics	Cardiovaccular Again Cardiovascular	Denression Anglesic	Oncology, Alzheimer's
as of January, 1999)	PHYSIOLOGY				Neurotransmitter	Gluconeogenesis	Neurotransmitter	Vascular Permeability	Neurotransmitter	Vacoconstriction	Vasodilation	Immune System	Chemoattractant	Chemoattractant	Cucinoalitaciani Fat Metabolism	Bronchodilator Dain	Motility Est About	Muscle Contraction	Metabolic Remiletion	Neurotransmitter	CNS	CNS	Neurotransmitter
(Receptors known as of January, 1999)	TISSUE				Brain, Nerves, Heart	Brain, Kidney, Lung Kidney, Heart	Brain, Kidney, GI	Vascular, Heart, Brain	IMOSI I ISSUES	Vascular, Liver, Kidney	Liver, Blood	Blood	Blood	Blood	Brain	Brain	Gastrointestinal	Heart, Bronchus, Brain	Kidney, Brain	Nerves, Intestine, Blood	Brain,	Brain,	Brain, Gastrointestinal
	NUMBER				3) 5	3 0		7	OT .	2	<del></del>	<del>,</del> ,	ი <del>-</del> -	9	7	1	2	2	5	5	<b>-</b>		n
	LIGAND	like	=	<ul> <li>Acetylcholine</li> </ul>	(muscarinic & nicotinic)  • Adrenoceptors	<ul><li>Alpha Adrenoceptors</li><li>Beta Adrenoceptors</li></ul>	•Dopamine •Histamina	Serotonin (5-HT)	•Peptide	• Angiotensin	•Bradykinin	• Coa anapnylatoxin • Fmet-len-nh•	Interleukin-8	• Chemokine	•Orexin	• Nociceptin	•CCK (Gastrin)	• Endothelin	• Melanocortin	•Neuropeptide Y	• Neurotensin	• Comptotition	Somatostatin.
	CLASS	Rhodopsin like	•								٠												



Depression, Analgesic Anti-coagulant, Anti-inflammatory Anti-diuretic, Diabetic Complications Analgesics, Alzheimer's	Infertility Infertility Thyroidism, Metabolism	Ophthalmic Diseases Olfactory Diseases	Cardiovascular, Analgesic Cancer, Anti-Inflammatory Cancer	Asthma, Rheumatoid Arthritis Cardiovascular Cardiovascular, Respiratory	Cardiovascular, Respiratory Cardiovascular, Respiratory Analgesics, Memory Anti-inflammatory, Anti-asthmatic	Prostate Cancer, Endometriosis	Metabolic Regulation Oncology, Alzheimer's Regulation of Circadian Cycle
Neurohormone Coagulation Water Balance Neurotransmitter	Endocrine Endocrine Endocrine	Photoreception Smell	Vasodilation, Pain Inflammation Cell proliferation	Inflammation Platelet Regulation Vasoconstriction	Multiple Effects Relaxes Muscle Sensory Perception Inflammation	Reproduction	Thyroid Regulation Neuroendocrine Neuroendocrine
Brain Nerves Platelets, Blood Vessels Arteries, Heart, Bladder Brain, Pancreas	Ovary, Testis Ovary, Testis Thyroid	5 Eye 4(~1000) Nose	Arterial, Gastrointestinal Vessels, Heart, Lung Most Cells White Blood Cells,	Bronchus Arterial, Gastrointestinal Arterial, Bronchus	Vascular, Bronchus Vascular, Platelets Brain Most Peripheral Tissues	Reproductive Organs, Pituitary	Pituitary, Brain Gastrointestinal Brain, Eye, Pituitary
υ ω 4 H	none 1 ropic 1	۶. ک	1 2 2 5	H H	4 4 4 4	lone 1	ne 1 actor 1
<ul> <li>Tachykinin (Substance P, NKA<sub>1</sub>)</li> <li>Thrombin</li> <li>Vasopressin-like</li> <li>Galanin</li> <li>Hormone protein</li> </ul>	lating horr riogonadot	•Opsin •Olfactory •Prostanoid	<ul> <li>Prostaglandin</li> <li>Lysophosphatidic Acid</li> <li>Sphingosine-1-phosphate</li> <li>Leukotriene</li> </ul>	<ul><li>Prostacyclin</li><li>Thromboxane</li><li>Nucleotide-like</li></ul>	<ul> <li>Adenosine</li> <li>Purinoceptors</li> <li>Cannabis</li> <li>Platelet activating factor</li> <li>Gonadotropin-releasing hormone like</li> </ul>	•Gonadotropin-releasing hormone	• Inviouopm-releasing hormone • Growth hormone-inhibiting factor • Melatonin

•Class II Secretin like

Obesity, Gastrointestinal Osteoporosis Stress, Mood, Obesity	Diabetes, Obesity Cardiovascular Cardiovascular, Diabetes, Obesity Growth Regulation	Osteoporosis Metabolic Regulation	Gastrointestinal	Hearing, Vision Mood Disorders Cataracts, GI Tumors
Digestion Calcium Resorption Neuroendocrine	Sugar/Fat Metabolism Gluconeogenesis Gluconeogenesis Neuroendocrine	Calcium Regulation Metabolism	Motility	Sensory Perception Neurotransmitter Calcium Regulation
Gastrointestinal, Heart Bone, Brain Adrenal, Vascular, Brain	Adrenals, Fat Cells Liver, Fat Cells, Heart Pancreas, Stomach, Lung Brain	Bone, Kidney Brain, Pancreas, Adrenals Metabolism	Gastrointestinal	Brain Brain Parathyroid, Kidney, GI Tract
Secretin     Calcitonin     Corticotropin releasing     factor/urocortin	•Gastric inhibitory peptide (GIP) 1 •Glucagon •Glucagon-like Peptide 1 (GLP-1) 1 •Growth hormone-releasing 1	•Parathyroid hormone 1 •PACAP 1 •Vasoactive intestinal	polypeptide (VIP) 1	•Metabotropic Glutamate 7 •GABA <sub>B</sub> 1 •Extracellular Calcium Sensing 1
	•		Class III	

### FIG. 3A

### G protein-coupled receptors:

(Division into Class A Or Class B)

- 1. A1 adenosine receptor [Homo sapiens]. ACCESSION AAB25533
  NPIVYAF RIQKFRVTFL KIWNDHFRCQ PAPPIDEDLP EERPDD
  Class A
- 2. adrenergic, alpha -1B-, receptor [Homo sapiens]. ACCESSION NP\_000670 npiiypc sskefkrafv rilgcqcrgr grrrrrrrr lggcaytyrp wtrggslers qsrkdsldds gsclsgsqrt lpsaspspgy lgrgapppve lcafpewkap gallslpape ppgrrgrhds gplftfkllt epespgtdgg asnggceaaa dvangqpgfk snmplapgqf

Class A

adrenergic receptor alpha-2A [Homo sapiens]. ACCESSION AAG00447
 npviytifn hdfrrafkki lcrgdrkriv

Class A

4. alpha-2B-adrenergic receptor - human. ACCESSION A37223 npviytifn qdfrrafiri lcrpwtqtaw

Class A

5. alpha-2C-adrenergic receptor - human. ACCESSION A31237 npviytvín qdfrpsíkhi lfrrrrgfr q
Class A

6. beta-1-adrenergic receptor [Homo sapiens]. ACCESSION NP\_000675 npiiyers pdfrkafqgl lccarraarr rhathgdrpr asgclarpgp ppspgaasdd ddddvvgatp parllepwag enggaaadsd ssldeperpg faseskv

Class A

7. beta-2 adrenergic receptor. ACCESSION P07550

npliyersp dfriafqell chrsslkay gngyssngnt 361 geqsgyhveq ekenkliced lpgtedfvgh qgtvpsdnid sqgrnestnd sll

Class A

8. dopamine receptor D1 [Homo sapiens]. ACCESSION NP\_000785
npii yafnadfrka fstllgcyrl cpatnnaiet vsinnngaam fsshheprgs iskecnlvyl iphavgssed lkkeeaagia
rpleklspal svildydtdv slekiqpitq ngqhpt

Class A

9. D(2) dopamine receptor. ACCESSION P14416
npiiyttfn iefrkaflki lhc
Class A

### FIG. 3B

10. d3 dopamine receptor - human. ACCESSION G01977 np viyttfnief rkaflkilsc

Class A

11. dopamine receptor D4 - human. ACCESSION DYHUD4 npviytv fnaefrnvfr kalracc

Class A

- dopamine receptor D5 human. ACCESSION DYHUD5

  npviya fnadfqkvfa qllgcshfcs rtpvetvnis nelisynqdi vfhkeiaaay ihmmpnavtp gnrevdndee egpfdrmfqi yqtspdgdpv aesvweldce geisldkitp ftpngfh

  Class A
- 13. muscarinic acetylcholine receptor M1 [Homo sapiens]. ACCESSION NP\_000729 npmcyal cnkafrdtfr llllcrwdkr rwrkipkrpg svhrtpsrqc
  Class A
- 14. muscarinic acetylcholine receptor M2 [Homo sapiens]. ACCESSION NP\_000730 npacy alcnatfkkt fkhllmchyk nigatr
  Class A
- 15. muscarinic acetylcholine receptor M3 [Homo sapiens]. ACCESSION NP\_000731 n pvcyalcnkt frttfkmlll eqedkkkrrk qqyqqrqsvi fhkrapeqal Class A
- 16. muscarinic acetylcholine receptor M4 [Homo sapiens]. ACCESSION NP\_000732 npa cyalenatfk ktfrhllleq yrnigtar

  Class A
- 17. m5 muscarinic receptor. locus HUMACHRM ACCESSION AAA51569 npicyalcnr tfrktfkmll lcrwkkkkve eklywqgnsk lp
  Class A
- 18. 5-hydroxytryptamine (serotonin) receptor 1A [Homo sapiens]. ACCESSION BAA90449 npviy ayfnkdfqna fkkiikckf
  Class A
- 19. 5-hydroxytryptamine (serotonin) receptor 1B [Homo sapiens]. ACCESSION BAA94455 npiiyt msnedfkqaf hklirfkcts
  Class A
- 20. 5-hydroxytryptamine (serotonin) receptor 1E [Homo sapiens]. ACCESSION BAA94458 n pllytsfned fklafkklir cre

Class A

### FIG. 3C

- 21. OLFACTORY RECEPTOR 6A1. ACCESSION 095222
  npiiyclmq evkralccil hlyqhqdpdp kkgsrnv
  Class A
- 22. OLFACTORY RECEPTOR 2C1. ACCESSION 095371 npliy tlrnmevkga lrrllgkgre vg
  Class A
- 23. angiotensin receptor 1 [Homo sapiens]. ACCESSION NP\_033611 npl fygflgkkfk ryflqllkyi ppkakshsnl sfkmsflsyr psdnvssstk kpapefeve Class B
- 24. angiotensin receptor 2 [Homo sapiens]. ACCESSION NP\_000677 npflycf vgnrfqqklr svfrvpitwl qgkresmscr kssslremet fvs Class B
- 25. interleukin 8 receptor beta (CXCR2) [Homo sapiens]. ACCESSION NM\_001557 NPLIYAFIGQKFRHGLLKILAIHGLISKDSLPKDSRPSFVGSSSGHTSTTL Class B
- 26. cx3c chemokine receptor 1 (cx3cr1) (fractalkine receptor) ACCESSION P49238 rnp liyafagekf rrylyhlygk clavlcgrsv hvdfsssesq rsrhgsvlss nftyhtsdgd allll Class B
- 27. neurotensin receptor human. ACCESSION S29506
  n pilynlvsan frhiflatla clcpvwrrrr krpafsrkad svssnhflss natretly
  Class B
- 28. SUBSTANCE-P RECEPTOR (SPR) (NK-1 RECEPTOR) (NK-1R). ACCESSION P25103 npiiycclnd rfrlgfkhaf rccpfisagd yeglemkstr ylqtqgsvyk vsrlettistvvgaheeepe dgpkatpssl dltsncssrs dsktmtesfs fssnvls Class B
- 29. vasopressin receptor type 2 [Homo sapiens]. ACCESSION AAD16444 npwiyasfss sysselrsll ccargrtpps lgpqdesctt assslakdts s

  Class B
- 30. thyrotropin-releasing hormone receptor human. ACCESSION JN0708
  npviy nlmsqkfraa frklenckqk ptekpanysv alnysvikes dhfstelddi tvtdtylsat kvsfddtela sevsfsqs
  Class B

### FIG. 3D

- 31. oxytocin receptor human. ACCESSION A55493
  npwiym lftghlfhel vqrflccsas ylkgrrlget saskksnsss fvlshrsssq rscsqpsta
  Class B
- 32. neuromedin U receptor [Homo sapiens]. ACCESSION AAG24793 npvlyslmssrfretfqealclgacchrlrprhsshslsrmttgstlcdvgslgswvhplagndgpeaqqetdps Class B
- 33. gastrin receptor. ACCESSION AAC37528
  nplvy cfmhrrfrqa cletcarccp rpprarpral pdedpptpsi aslsrlsytt istlgpg
  Class B
- 34. galanin receptor 3 [Homo sapiens]. ACCESSION 10879541
  nplv yalasrhfra rfirlwpcgr nrhrarral rrvrpassgp pgcpgdarps grllagggqg pepregpvhg geaargpe
  Class A
- 35. edg-1 human. ACCESSION A35300
  npiiy tltnkemrra firimsceke psgdsagkfk rpiiagmefs rsksdnsshp 361 qkdegdnpet imssgnvnss s
  Class A
- 36. central cannabinoid receptor [Homo sapiens]. ACCESSION NP\_057167 npiiyalr skdlrhafrs mfpscegtaq pldnsmgdsd clhkhannaa svhraaesci kstvkiakvt msvstdtsae al Class A
- 37. delta opioid receptor human. ACCESSION I38532
  npvlyaf ldenfkrcfr qlcrkpcgrp dpssfsrpre atarervtac tpsdgpgggr aa
  Class A
- 38. proteinase activated receptor 2 (PAR-2) human. ACCESSION P55085 dpfvyyfvshdfrdhaknallcrsvrtvkqmqvsltskkhsrksssyssssttvktsy

  Class A
- 39. vasopressive intestinal peptide receptor (VIPR) rat. ACCESSION NM\_012685
  NGEVQAELRRKWRRWHLQGVLGWSSKSQHPWGGSNGATCSTQVSMLTRVSPSARR
  SSSFQAEVSLV

Class B

#### FIG. 4A

The mutated amino acid at the second position of the DRY motif is underlined.

VASOPRESSIN V2 RECEPTOR - (Human) accession P30518

#### R137H

1 MLMASTTSAV PGHPSLPSLP SNSSQERPLD TRDPLLARAE LALLSIVFVA VALSNGLVLA 61 ALARRGRRGH WAPIHVFIGH LCLADLAVAL FQVLPQLAWK ATDRFRGPDA LCRAVKYLQM 121 VGMYASSYMI LAMTLDHHRA ICRPMLAYRH GSGAHWNRPV LVAWAFSLLL SLPQLFIFAQ 181 RNVEGGSGVT DCWACFAEPW GRRTYVTWIA LMVFVAPTLG IAACQVLIFR EIHASLVPGP 241 SERPGGRRG RRTGSPGEGA HVSAAVAKTV RMTLVIVVVY VLCWAPFFLV QLWAAWDPEA 301 PLEGAPFVLL MLLASLNSCT NPWIYASFSS SVSSELRSLL CCARGRTPPS LGPQDESCTT 361 ASSSLAKDTS S

## ALPHA-1B ADRENERGIC RECEPTOR (ALPHA 1B-ADRENOCEPTOR). (Golden hamster) ACCESSION P18841

### **R143E**

- 1 MNPDLDTGHN TSAPAQWGEL KDANFTGPNQ TSSNSTLPQL DVTRAISVGL VLGAFILFAI 61 VGNILVILSV ACNRHLRTPT NYFIVNLAIA DLLLSFTVLP FSATLEVLGY WVLGRIFCDI 121 WAAVDVLCCT ASILSLCAIS IDEYIGVRYS LQYPTLVTRR KAILALLSVW VLSTVISIGP
- 181 LLGWKEPAPN DDKECGVTEE PFYALFSSLG SFYIPLAVIL VMYCRVYIVA KRTTKNLEAG
- 241 VMKEMSNSKE LTLRIHSKNF HEDTLSSTKA KGHNPRSSIA VKLFKFSREK KAAKTLGIVV 301 GMFILCWLPF FIALPLGSLF STLKPPDAVF KVVFWLGYFN SCLNPIIYPC SSKEFKRAFM
- 361 RILGCQCRSG RRRRRRRLG ACAYTYRPWT RGGSLERSQS RKDSLDDSGS CMSGSQRTLP
- 421 SASPSPGYLG RGAQPPLELC AYPEWKSGAL LSLPEPPGRR GRLDSGPLFT FKLLGEPESP
- 481 GTEGDASNGG CDATTDLANG QPGFKSNMPL APGHF

(SEQ ID NO:41)

#### R143A

- 1 MNPDLDTGHN TSAPAQWGEL KDANFTGPNQ TSSNSTLPQL DVTRAISVGL VLGAFILFAI
- 61 VGNILVILSV ACNRHLRTPT NYFIVNLAIA DLLLSFTVLP FSATLEVLGY WVLGRIFCDI
- 121 waavdvlcct asilslcais id $\underline{\underline{\mathbf{A}}}$ yigvrys lqyptlvtrr kailallsvw vlstvisigp
- 181 LLGWKEPAPN DDKECGVTEE PFYALFSSLG SFYIPLAVIL VMYCRVYIVA KRTTKNLEAG
- 241 VMKEMSNSKE LTLRIHSKNF HEDTLSSTKA KGHNPRSSIA VKLFKFSREK KAAKTLGIVV
- 301 GMFILCWLPF FIALPLGSLF STLKPPDAVF KVVFWLGYFN SCLNPIIYPC SSKEFKRAFM
- 361 RILGCQCRSG RRRRRRRLG ACAYTYRPWT RGGSLERSQS RKDSLDDSGS CMSGSQRTLP 421 SASPSPGYLG RGAQPPLELC AYPEWKSGAL LSLPEPPGRR GRLDSGPLFT FKLLGEPESP
- 481 GTEGDASNGG CDATTDLANG OPGFKSNMPL APGHF

(SEQ ID NO:42)

#### FIG. 4B

#### R143H

MNPDLDTGHN TSAPAQWGEL KDANFTGPNQ TSSNSTLPQL DVTRAISVGL VLGAFILFAI
61 VGNILVILSV ACNRHLRTPT NYFIVNLAIA DLLLSFTVLP FSATLEVLGY WVLGRIFCDI
121 WAAVDVLCCT ASILSLCAIS IDHYIGVRYS LQYPTLVTRR KAILALLSVW VLSTVISIGP
181 LLGWKEPAPN DDKECGVTEE PFYALFSSLG SFYIPLAVIL VMYCRVYIVA KRTTKNLEAG
241 VMKEMSNSKE LTLRIHSKNF HEDTLSSTKA KGHNPRSSIA VKLFKFSREK KAAKTLGIVV
301 GMFILCWLPF FIALPLGSLF STLKPPDAVF KVVFWLGYFN SCLNPIIYPC SSKEFKRAFM
361 RILGCQCRSG RRRRRRLG ACAYTYRPWT RGGSLERSQS RKDSLDDSGS CMSGSQRTLP
421 SASPSPGYLG RGAQPPLELC AYPEWKSGAL LSLPEPPGRR GRLDSGPLFT FKLLGEPESP
481 GTEGDASNGG CDATTDLANG QPGFKSNMPL APGHF

### **R143N**

1 MNPDLDTGHN TSAPAQWGEL KDANFTGPNQ TSSNSTLPQL DVTRAISVGL VLGAFILFAI
61 VGNILVILSV ACNRHLRTPT NYFIVNLAIA DLLLSFTVLP FSATLEVLGY WVLGRIFCDI
121 WAAVDVLCCT ASILSLCAIS IDNYIGVRYS LQYPTLVTR KAILALLSVW VLSTVISIGP
181 LLGWKEPAPN DDKECGVTEE PFYALFSSLG SFYIPLAVIL VMYCRVYIVA KRTTKNLEAG
241 VMKEMSNSKE LTLRIHSKNF HEDTLSSTKA KGHNPRSSIA VKLFKFSREK KAAKTLGIVV
301 GMFILCWLPF FIALPLGSLF STLKPPDAVF KVVFWLGYFN SCLNPIIYPC SSKEFKRAFM
361 RILGCQCRSG RRRRRRRIG ACAYTYRPWT RGGSLERSQS RKDSLDDSGS CMSGSQRTLP
421 SASPSPGYLG RGAQPPLELC AYPEWKSGAL LSLPEPPGRR GRLDSGPLFT FKLLGEPESP
481 GTEGDASNGG CDATTDLANG QPGFKSNMPL APGHF

(SEQ ID NO:44)

FIG. 4C

### Angiotensin II Receptor, Type 1 (AT1A) [Rattus norvegicus]. ACCESSION NP\_112247

### R126H

- 1 MALNSSAEDG IKRIQDDCPK AGRHSYIFVM IPTLYSIIFV VGIFGNSLVV IVIYFYMKLK
- 61 TVASVFLLNL ALADLCFLLT CPLWAVYTAM EYRWPFGNHL CKIASASVTF NLYASVFLLT
- 121 CLSID $\underline{\mathbf{H}}$ YLAI VHPMKSRLRR TMLVAKVTCI IIWLMAGLAS LPAVIHRNVY FIENTNITVC
- 181 AFHYESRNST LPIGLGLTKN ILGFLFPFLI ILTSYTLIWK ALKKAYEIQK NKPRNDDIFR
- 241 IIMAIVLFFF FSWVPHQIFT FLDVLIQLGV IHDCKISDIV DTAMPITICI AYFNNCLNPL
- 301 FYGFLGKKFK KYFLQLLKYI PPKAKSHSSL STKMSTLSYR PSDNMSSSAK KPASCFEVE (SEQ ID NO:45)

#### **FIGS. 5A - 5B**

### A. Amino Acid sequence of the hGPR3- Enhanced Receptor

MMWGAGSPLAWLSAGSGNVNVSSVGPAEGPTGPAAPLPSPKAWDVVLCISGTLVSCENA LVVAIIVGTPAFRAPMFLLVGSLAVADLLAGLGLVLHFAAVFCIGSAEMSLVLVGVLAM AFTASIGSLLAITVDRYLSLYNALTYYSETTVTRTYVMLALVWGGALGLGLLPVLAWNC LDGLTTCGVVYPLSKNHLVVLAIAFFMVFGIMLQLYAQICRIVCRHAQQIALQRHLLPA SHYVATRKGIATLAVVLGAFAACWLPFTVYCLLGDAHSPPLYTYLTLLPATYNSMINPI IYAFRNQDVQKVLWAVCCCCAAARGRTPPSLGPQDESCTTASSSLAKDTSS (SEQ ID No: 46)

### B. Nucleotide sequence of the hGPR3- Enhanced Receptor

ATGATGTGGGGTGCAGGCAGCCCTCTGGCCTGGCTCAGCTGGCTCAGGCAACGTGAA TGTAAGCAGCGTGGGCCCAGCAGAGGGGCCCACAGGTCCAGCCGCACCACTGCCCTCGC CTAAGGCCTGGGATGTGGTGCTCTGCATCTCAGGCACCCTGGTGTCCTGCGAGAATGCG CTAGTGGTGGCCATCATCGTGGGCACTCCTGCCTTCCGTGCCCCCATGTTCCTGCTGGT GGGCAGCCTGGCCGTGGCAGACCTGCTGGCAGGCCTGGGCCTGGTCCTGCACTTTGCTG CTGTCTTCTGCATCGGCTCAGCGGAGATGAGCCTGGTGCTGGTTGGCGTGCTGGCAATG GCCTTTACYGCCAGCATCGGCAGTCTACTGGCCATCACTGTCGACCGCTACCTTTCTCT GTACAATGCCCTCACCTACTATTCAGAGACAACAGTGACACGGACCTATGTGATGCTGG  $\tt CCTTAGTGTGGGGGGGTGCCTGGGGCCTGGGGCCTGGGAACTGC$  $\tt CTGGATGGCCTGACCACTGTGGCGTGGTTTATCCACTCTCCAAGAACCATCTGGTAGT$ TCTGGCCATTGCCTTCTTCATGGTGTTTTGGCATCATGCTGCAGCTCTACGCCCAAATCT TCCCACTATGTGGCCACCCGCAAGGGCATTGCCACACTGGCCGTGGTGCTTGGAGCCTT TGCCGCCTGCTGGTTGCCCTTCACTGTCTACTGCCTGGGTGATGCCCACTCTCCAC CTCTCTACACCTATCTTACCTTGCTCCCTGCCACCTACAACTCCATGATCAACCCTATC ATCTACGCCTTCCGCAACCAGGATGTGCAGAAAGTGCTGTGGGGCTGTCTGCTGCTG TGCGGCCGCACGCACCCACCCAGCCTGGGTCCCCAAGATGAGTCCTGCACCA CCGCCAGCTCCTCCCTGGCCAAGGACACTTCATCGTGA

(SEQ ID No: 47)

### FIGS. 5C - 5D

### C. Amino Acid sequence of the hGPR6- Enhanced Receptor

MNASAASLNDSQVVVVAAEGAAAAATAAGGPDTGEWGPPAAAALGAGGGANGSLELSSQ LSAGPPGLLLPAVNPWDVLLCVSGTVIAGENALVVALIASTPALRTPMFVLVGSLATAD LLAGCGLILHFVFQYLVPSETVSLLTVGFLVASFAASVSSLLAITVDRYLSLYNALTYY SRRTLLGVHLLLAATWTVSLGLGLLPVLGWNCLAERAACSVVRPLARSHVALLSAAFFM VFGIMLHLYVRICQVVWRHAHQIALQQHCLAPPHLAATRKGVGTLAVVLGTFGASWLPF AIYCVVGSHEDPAVYTYATLLPATYNSMINPIIYAFRNQEIQRALWLLLCGCAAARGRT PPSLGPQDESCTTASSSLAKDTSS (SEQ ID No: 48)

### D. Nucleotide sequence of the hGPR6- Enhanced Receptor

ATGAACGCGAGCGCCCCCCCCAACGACTCCCAGGTGGTGGTAGTGGCGGCCGAAGG AGCGGCGGCGGCCACAGCAGCAGGGGGGGCCGACACGGCGAATGGGGACCCCCTG CTGCGGCGCTCTAGGAGCCGGCGGCGAGCTAATGGGTCTCTGGAGCTGTCCTCGCAG CTGTCGGCTGGGCCACCGGGACTCCTGCTGCCAGCGGTGAATCCGTGGGACGTGCTCCT GTGCGTGTCGGGGACAGTGATCGCTGGAGAAAACGCGCTGGTGGTGGCGCTCATCGCGT CCACTCCGGCGCTGCCACGCCCATGTTCGTGCTGGTAGGCAGCCTGGCCACCGCTGAC CTGTTGGCGGGCTGTGGCCTCATCTTGCACTTTGTGTTCCAGTACTTGGTGCCCTCGGA GACTGTGAGTCTCCTCGTGGCCTCCTTCGCCGCCTCTGTCAGCA GCCTGCTGGCCATTACGGTGGACCGCTACCTGTCCCTGTATAACGCGCTCACCTATTAC TCGCGCCGGACCCTGTTGGGCGTGCACCTCCTGCTTGCCGCCACTTGGACCGTGTCCCT AGGCCTGGGGCTGCCGCTGCTGGGCTGGAACTGCCTGGCAGAGCGCCGCCTGCA GTCTTCGGCATCATGCTGCACCTGTACGTGCGCATCTGCCAGGTGGTCTGGCGCCACGC GCACCAGATCGCGCTGCAGCAGCACTGCCTGGCGCCACCCCATCTCGCTGCCACCAGAA GCCATCTATTGCGTGGTGGGCAGCCATGAGGACCCGGCGGTCTACACTTACGCCACCCT GCTGCCCGCCACCTACAACTCCATGATCAATCCCATCATCTATGCCTTCCGCAACCAGG  ${\tt CCACCCAGCCTGGGTCCCCAAGATGAGTCCTGCACCACCGCCAGCTCCTCGCCAA}$ GGACACTTCATCGTGA

(SEQ ID No: 49)

### FIGS. 5E - 5F

### E. Amino Acid sequence of the hGPR12- Enhanced Receptor

MNEDLKVNLSGLPRDYLDAAAAENISAAVSSRVPAVEPEPELVVNPWDIVLCTSGTLIS CENAIVVLIIFHNPSLRAPMFLLIGSLALADLLAGIGLITNFVFAYLLQSEATKLVTIG LIVASFSASVCSLLAITVDRYLSLYYALTYHSERTVTFTYVMLVMLWGTSICLGLLPVM GWNCLRDESTCSVVRPLTKNNAAILSVSFLFMFALMLQLYIQICKIVMRHAHQIALQHH FLATSHYVTTRKGVSTLAIILGTFAACWMPFTLYSLIADYTYPSIYTYATLLPATYNSI INPVIYAFRNQEIQKALCLICCGCAAARGRTPPSLGPQDESCTTASSSLAKDTSS (SEQ ID No: 50)

### F. Nucleotide sequence of the hGPR12- Enhanced Receptor

ATGAATGAAGACCTGAAGGTCAATTTAAGCGGGCTGCCTCGGGATTATTTAGATGCCGC TGCTGCGGAGAACATCTCGGCTGCTGTCTCCTCCGGGTTCCTGCCGTAGAGCCAGAGC CTGAGCTCGTAGTCAACCCCTGGGACATTGTCTTGTGTACCTCGGGAACCCTCATCTCC TGTGAAAATGCCATTGTGGTCCTTATCATCTTCCACAACCCCAGCCTGCGAGCACCCAT GTTCCTGCTAATAGGCAGCCTGGCTCTTGCAGACCTGCTGGCCGGCATTGGACTCATCA  ${\tt CCAATTTTGTTTTTGCCTACCTGCTTCAGTCAGAAGCCACCAAGCTGGTCACGATCGGC}$ CTCATTGTCGCCTCTTTCTCTGCCTCTGTCTGCAGCTTGCTGGCTATCACTGTTGACCG CTACCTCTCACTGTACTACGCTCTGACGTACCATTCGGAGAGGACGGTCACGTTTACCT ATGTCATGCTCGTCATGCTCTGGGGGACCTCCATCTGCCTGGGGCTGCTGCCCGTCATG GGCTGGAACTGCCTCCGAGACGAGTCCACCTGCAGCGTGGTCAGACCGCTCACCAAGAA CAACGCGGCCATCCTCGGTGTCCTTCCTCTTCATGTTTGCGCTCATGCTTCAGCTCT ACATCCAGATCTGTAAGATTGTGATGAGGCACGCCCATCAGATAGCCCTGCAGCACCAC TTCCTGGCCACGTCGCACTATGTGACCACCCGGAAAGGGGTCTCCACCCTGGCTATCAT  ${\tt CCTGGGGACGTTTGCTGCTTGGATGCCTTTCACCCTCTATTCCTTGATAGCGGATT}$ ACACCTACCCCTCCATCTATACCTACGCCACCCTCCTGCCCGCCACCTACAATTCCATC ATCAACCCTGTCATATATGCTTTCAGAAACCAAGAGATCCAGAAAGCGCTCTGTCTCAT TTGCTGCGGCTGCGCGCCCCACGCGCACCCCACCCAGCCTGGGTCCCCAAGATG AGTCCTGCACCACCGCCAGCTCCTCCCTGGCCAAGGACACTTCATCGTGA (SEQ ID No: 51)

### FIGS. 5G - 5H

### G. Amino Acid sequence of the hSREB3- Enhanced Receptor

MANTTGEPEEVSGALSPPSASAYVKLVLLGLIMCVSLAGNAILSLLVLKERALHKAPYY FLLDLCLADGIRSAVCFPFVLASVRHGSSWTFSALSCKIVAFMAVLFCFHAAFMLFCIS VTRYMAIAHHRFYAKRMTLWTCAAVICMAWTLSVAMAFPPVFDVGTYKFIREEDQCIFE HRYFKANDTLGFMLMLAVLMAATHAVYGKLLLFEYRHRKMKPVQMVPAISQNWTFHGPG ATGQAAANWIAGFGRGPMPPTLLGIRQNGHAASRRLLGMDEVKGEKQLGRMFYAITLLF LLLWSPYIVACYWRVFVKACAVPHRYLATAVWMSFAQAAVNPIVCFLLNKDLKKCLRTH APCAAARGRTPPSLGPQDESCTTASSSLAKDTSS (SEQ ID No: 52)

### H. Nucleotide sequence of the hSREB3- Enhanced Receptor

ATGGCCAACACTACCGGAGAGCCTGAGGAGGTGAGCGGCGCTCTGTCCCCACCGTCCGC ATCAGCTTATGTGAAGCTGGTACTGCTGGGACTGATTATGTGCGTGAGCCTGGCGGGTA ACGCCATCTTGTCCCTGCTGGTGCTCAAGGAGCGTGCCCTGCACAAGGCTCCTTACTAC  ${\tt TTCCTGCTGGACCTGTGCCTGGCCGATGGCATACGCTCTGCCGTCTGCTTTGT}$ GCTGGCTTCTGTGCGCCACGGCTCTTCATGGACCTTCAGTGCACTCAGCTGCAAGATTG TGGCCTTTATGGCCGTGCTCTTTTGCTTCCATGCGGCCTTCATGCTGTTCTGCATCAGC GTCACCCGCTACATGGCCATCGCCCACCACCGCTTCTACGCCAAGCGCATGACACTCTG CATCGCTACTTCAAGGCCAATGACACGCTGGGCTTCATGCTTATGTTGGCTGTGCTCAT GGCAGCTACCCATGCTGTCTACGGCAAGCTGCTCCTCTTCGAGTATCGTCACCGCAAGA  ${\tt TGAAGCCAGTGCAGATGGTGCCAGCCATCAGCCAGAACTGGACATTCCATGGTCCCGGG}$ GCCACCGGCCAGGCTGCCGAACTGGATCGCCGGCTTTGGCCGTGGGCCCATGCCACC ACGAGGTCAAGGGTGAAAAGCAGCTGGGCCGCATGTTCTACGCGATCACACTGCTCTTT CTGCTCCTCTGGTCACCCTACATCGTGGCCTGCTACTGGCGAGTGTTTGTGAAAGCCTG TGCTGTGCCCCACCGCTACCTGGCCACTGCTGTTTGGATGAGCTTCGCCCAGGCTGCCG GCCCCCTGCGCGCCCCCCGGGGACGCACCCCACCCAGCCTGGGTCCCCAAGATGAGTC CTGCACCACCGCCAGCTCCTCCCTGGCCAAGGACACTTCATCGTGA (SEQ ID No: 53)

### FIGS. 51 - 5J

### I. Amino Acid sequence of the hSREB2- Enhanced Receptor

MANYSHAADNILQNLSPLTAFLKLTSLGFIIGVSVVGNLLISILLVKDKTLHRAPYYFL LDLCCSDILRSAICFPFVFNSVKNGSTWTYGTLTCKVIAFLGVLSCFHTAFMLFCISVT RYLAIAHHRFYTKRLTFWTCLAVICMVWTLSVAMAFPPVLDVGTYSFIREEDQCTFQHR SFRANDSLGFMLLLALILLATQLVYLKLIFFVHDRRKMKPVQFVAAVSQNWTFHGPGAS GQAAANWLAGFGRGPTPPTLLGIRQNANTTGRRRLLVLDEFKMEKRISRMFYIMTFLFL TLWGPYLVACYWRVFARGPVVPGGFLTAAVWMSFAQAGINPFVCIFSNRELRRCFSTTL LYCAAARGRTPPSLGPQDESCTTASSSLAKDTSS (SEQ ID No: 54)

### J. Nucleotide sequence of the hSREB2- Enhanced Receptor

ATGCCGAACTATAGCCATGCAGCTGACAACATTTTGCAAAATCTCTCGCCTCTAACAGC CTTTCTGAAACTGACTTCCTTGGGTTTCATAATAGGAGTCAGCGTGGTGGGCAACCTCC TGATCTCCATTTTGCTAGTGAAAGATAAGACCTTGCATAGAGCACCTTACTACTTCCTG TTGGATCTTTGCTGTTCAGATATCCTCAGATCTGCAATTTGTTTTCCCATTTGTGTTCAA CTCTGTCAAAAATGGCTCTACCTGGACTTATGGGACTCTGACTTGCAAAGTGATTGCCT TTCTGGGGGTTTTGTCCTGTTTCCACACTGCTTTCATGCTCTTCTGCATCAGTGTCACC AGATACTTAGCTATCGCCCATCACCGCTTCTATACAAAGAGGCTGACCTTTTGGACGTG TCTGGCTGTGATCTGTATGGTGTGGACTCTGTCTGTGGCCATGGCATTTCCCCCGGTTT TAGACGTGGGCACTTACTCATTCATTAGGGAGGAAGATCAATGCACCTTCCAACACCGC TCCTTCAGGGCTAATGATTCCTTAGGATTTATGCTGCTTCTtGCTCCTCATCCTCCTAGC CACACAGCTTGTCTACCTCAAGCTGATATTTTTCGTCCACGATCGAAGAAAATGAAGC CAGTCCAGTTTGTAGCAGCAGTCAGCCAGAACTGGACTTTTCATGGTCCTGGAGCCAGT GCTGGGCATCAGGCAAAATGCAAACACCACAGGCAGAAGAAGGCTATTGGTCTTAGACG AGTTCAAAATGGAGAAAAGAATCAGCAGAATGTTCTATATAATGACTTTTCTGTTTCTA ACCTTGTGGGGCCCCTACCTGGTGGCCTGTTATTGGAGAGTTTTTTGCAAGAGGGCCTGT AGTACCAGGGGGATTTCTAACAGCTGCTGTCTGGATGAGTTTTGCCCAAGCAGGAATCA ATCCTTTTGTCTGCATTTTCTCAAACAGGGAGCTGAGGCGCTGTTTCAGCACAACCCTT CTTTACTGCGCGGCCCCCGGGGACGCACCCCACCCAGCCTGGGTCCCCAAGATGAGTC CTGCACCACCGCCAGCTCCTCCCTGGCCAAGGACACTTCATCGTGA (SEQ ID No: 55)

#### **FIGS. 5K - 5L**

### K. Amino Acid sequence of the hGPR8- Enhanced Receptor

MQAAGHPEPLDSRGSFSLPTMGANVSQDNGTGHNATFSEPLPFLYVLLPAVYSGICAVG LTGNTAVILVILRAPKMKTVTNVFILNLAVADGLFTLVLPVNIAEHLLQYWPFGELLCK LVLAVDHYNIFSSIYFLAVMSVDRYLVVLATVRSRHMPWRTYRGAKVASLCVWLGVTVL VLPFFSFAGVYSNELQVPSCGLSFPWPERVWFKASRVYTLVLGFVLPVCTICVLYTDLL RRLRAVRLRSGAKALGKARRKVTVLVLVVLAVCLLCWTPFHLASVVALTTDLPQTPLVI SMSYVITSLSYANSCLNPFLYAFLDDNFRKNFRSILRCAAARGRTPPSLGPQDESCTTA SSSLAKDTSS

(SEQ ID No: 56)

### L. Nucleotide sequence of the hGPR8- Enhanced Receptor

GATGGGTGCCAACGTCTCTCAGGACAATGGCACTGGCCACAATGCCACCTTCTCCGAGC CACTGCCGTTCCTCTATGTGCTCCTGCCCGCCGTGTACTCCGGGATCTGTGCTGTGGGG CTGACTGGCAACACGGCCGTCATCCTTGTAATCCTAAGGGCGCCCCAAGATGAAGACGGT GACCAACGTGTTCATCCTGAACCTGGCCGTCGCCGACGGGCTCTTCACGCTGGTACTGC  ${ t CCGTCAACATCGCGGAGCACCTGCTGCAGTACTGGCCCTTCGGGGAGCTGCTCTGCAAG$ CTGGTGCTGGCCGTCGACCACTACAACATCTTCTCCAGCATCTACTTCCTAGCCGTGAT GAGCGTGGACCGATACCTGGTGGTGCTGGCCACCGTGAGGTCCCGCCACATGCCCTGGC GTTCTGCCCTTCTTCTCTTTCGCTGGCGTCTACAGCAACGAGCTGCAGGTCCCAAGCTG TGGGCTGAGCTTCCCGTGGCCCGAGCGGGTCTGGTTCAAGGCCAGCCGTGTCTACACTT TGGTCCTGGGCTTCGTGCCCGTGTGCACCATCTGTGTGCTCTACACAGACCTCCTG CGCAGGCTGCGGGCCGCTCCGCTCTGGAGCCAAGGCTCTAGGCAAGGCCAGGCG GAAGGTGACCGTCCTGGTCCTCGTGCTGCCGTGTGCCTCCTCTGCTGGACGCCCT TCCACCTGGCCTCTGTCGTGGCCCTGACCACGGACCTGCCCCAGACCCCACTGGTCATC AGTATGTCCTACGTCATCACCAGCCTCAGCTACGCCAACTCGTGCCTGAACCCCTTCCT CTACGCCTTTCTAGATGACAACTTCCGGAAGAACTTCCGCAGCATATTGCGGTGCGCGG CCGCACGGGGACGCACCCAGCCTGGGTCCCCAAGATGAGTCCTGCACCACCGCC AGCTCCTCCCTGGCCAAGGACACTTCATCGTGA

(SEQ ID No: 57)

### FIGS. 5M - 5N

### M. Amino Acid sequence of the hGPR22-Enhanced Receptor

MCFSPILEINMQSESNITVRDDIDDINTNMYQPLSYPLSFQVSLTGFLMLEIVLGLGSN LTVLVLYCMKSNLINSVSNIITMNLHVLDVIICVGCIPLTIVILLLSLESNTALICCFH EACVSFASVSTAINVFAITLDRYDISVKPANRILTMGRAVMLMISIWIFSFFSFLIPFI EVNFFSLQSGNTWENKTLLCVSTNEYYTELGMYYHLLVQIPIFFFTVVVMLITYTKILQ ALNIRIGTRFSTGQKKKARKKKTISLTTQHEATDMSQSSGGRNVVFGVRTSVSVIIALR RAVKRHRERRERQKRVFRMSLLIISTFLLCWTPISVLNTTILCLGPSDLLVKLRLCFLV MAYGTTIFHPLLYAFTRQKFQKVLKSKMKKRVVCAAARGRTPPSLGPQDESCTTASSSL AKDTSS

(SEQ ID No: 58)

### N. Nucleotide sequence of the hGPR22-Enhanced Receptor

ATGTGTTTTTCTCCcaTTCTGGAAATCAACATGCAGTCTGAATCTAACATTACAGTGCG TTCAAGTGTCTCTCACCGGATTTCTTATGTTAGAAATTGTGTTGGGACTTGGCAGCAAC CTCACTGTATTGGTACTTACTGCATGAAATCCAACTTAATCAACTCTGTCAGTAACAT TATTACAATGAATCTTCATGTACTTGATGTAATAATTTGTGTGGGATGTATTCCTCTAA CTATAGTTATCCTTCTGCTTTCACTGGAGAGTAACACTGCTCTCATTTGCTGTTTCCAT GAGGCTTGTGTATCTTTTGCAAGTGTCTCAACAGCAATCAACGTTTTTGCTATCACTTT GGACAGATATGACATCTCTGTAAAACCTGCAAACCGAATTCTGACAATGGGCAGAGCTG TAATGTTAATGATATCCATTTGGATTTTTTTTTTTTTTCTCTTTTCCTGATTCCTTTTATT GAGGTAAATTTTTTCAGTCTTCAAAGTGGAAATACCTGGGAAAACAAGACACTTTTATG TGTCAGTACAAATGAATACTACACTGAACTGGGAATGTATTATCACCTGTTAGTACAGA TCCCAATATTCTTTTTCACTGTTGTAGTAATGTTAATCACATACACCAAAATACTTCAG GCTCTTAATATTCGAATAGGCACAAGATTTTCAACAGGGCAGAAGAAGCAAGAAA GAAAAAGACAATTTCTCTAACCACACAACATGAGGCTACAGACATGTCACAAAGCAGTG GTGGGAGAAATGTAGTCTTTGGTGTAAGAACTTCAGTTTCTGTAATAATTGCCCTCCGG CGAGCTGTGAAACGACACCGTGAACGACGAGAAAGACAAAAGAGAGTCTTCAGGATGTC TTTATTGATTATTTCTACATTTCTTCTCTGCTGGACACCAATTTCTGTTTTAAATACCA  ${\tt CCATTTTATGTTTAGGCCCAAGTGACCTTTTAGTAAAATTAAGATTGTGTTTTTTAGTC}$ ATGGCTTATGGAACAACTATATTTCACCCTCTATTATATGCATTCACTAGACAAAAATT GCACCCCACCCAGCCTGGGTCCCCAAGATGAGTCCTGCACCACCGCCAGCTCCTCCCTG GCCAAGGACACTTCATCGTGA

(SEQ ID No: 59)

### FIGS. 6A - 6C

### A. Amino acid sequence of the $\beta_2AR$ -V2R chimera

MGQPGNGSAFLLAPNRSHAPDHDVTQQRDEVWVVGMGIVMSLIVLAIVFGNVLVITAI AKFERLQTVTNYFITSLACADLVMGLAVVPFGAAHILMKMWTFGNFWCEFWTSIDVLC VTASIETLCVIAVDRYFAITSPFKYQSLLTKNKARVIILMVWIVSGLTSFLPIQMHWYRAT HQEAINCYANETCCDFFTNQAYAIASSIVSFYVPLVIMVFVYSRVFQEAKRQLQKIDKSE GRFHVQNLSQVEQDGRTGHGLRRSSKFCLKEHKALKTLGIIMGTFTLCWLPFFIVNIVHV IQDNLIRKEVYILLNWIGYVNSGFNPLIYCRSPDFRIAFQELLCARGRTPPSLGPQDESCTT ASSSLAKDTSS (Seq. ID No. 60)

### B. Amino acid sequence of the MOR-V2R chimera

MDSSTGPGNTSDCSDPLAQASCSPAPGSWLNLSHVDGNQSDPCGLNRTGLGGNDSLCP QTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADALAT STLPFQSVNYLMGTWPFGTILCKIVISIDYYNMFTSIFTLCTMSVDRYIAVCHPVKALDFR TPRNAKIVNVCNWILSSAIGLPVMFMATTKYRQGSIDCTLTFSHPTWYWENLLKICVFIF AFIMPILIITVCYGLMILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVFIVCWTPIHIYVI IKALITIPETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENFKRCFREFCAAARGRTPPSL **GPQDESCTTASSSLAKDTSS** (Seq. ID No. 61)

### C. Amino acid sequence of the D1AR-V2R chimera

 ${\bf MAPNTSTMDEAGLPAERDFSFRILTACFLSLLILSTLLGNTLVCAAVIRFRHLRSKVTNFF}$ VISLAVSDLLVAVLVMPWKAVAEIAGFWPFGSFCNIWVAFDIMCSTASILNLCVISVDRY WAISSPFQYERKMTPKAAFILISVAWTLSVLISFIPVQLSWHKAKPTWPLDGNFTSLEDTE DDNCDTRLSRTYAISSSLISFYIPVAIMIVTYTSIYRIAQKQIRRISALERAAVHAKNCQTT AGNGNPVECAQSESSFKMSFKRETKVLKTLSVIMGVFVCCWLPFFISNCMVPFCGSEET QPFCIDSITFDVFVWFGWANSSLNPIIYAFNADFQKAFSTLLGCYRLCAAARGRTPPSLGP **QDESCTTASSSLAKDTSS** 

(Seq. ID No. 62)

#### FIGS. 6D - 6F

### D. Amino acid sequence of the 5HT1AR-V2R chimera

MDVLSPGQGNNTTSPPAPFETGGNTTGISDVTVSYQVITSLLLGTLIFCAVLGNACVVAA IALERSLQNVANYLIGSLAVTDLMVSVLVLPMAALYQVLNKWTLGQVTCDLFIALDVL CCTSSILHLCAIALDRYWAITDPIDYVNKRTPRRAAALISLTWLIGFLISIPPMLGWRTPED RSDPDACTISKDHGYTIYSTFGAFYIPLLIMLVLYGRIFRAARFRIRKTVKKVEKTGADT RHGASPAPQPKKSVNGESGSRNWRLGVESKAGGALCANGAVRQGDDGAALEVIEVHR VGNSKEHLPLPSEAGPTPCAPASFERKNERNAEAKRKMALARERKTVKTLGIIMGTFILC WLPFFIVALVLPFCESSCHMPTLLGAIINWLGYSNSLLNPVIYAYFNKDFQNAFKKIIKCN FCAAARGRTPPSLGPQDESCTTASSSLAKDTSS (Seq. ID No. 63)

### E. Amino acid sequence of the β3AR-V2R chimera

MAPWPHENSSLAPWPDLPTLAPNTANTSGLPGVPWEAALAGALLALAVLATVGGNLLV IVAIAWTPRLQTMTNVFVTSLAAADLVMGLLVVPPAATLALTGHWPLGATGCELWTSV DVLCVTASIETLCALAVDRYLAVTNPLRYGALVTKRCARTAVVLVWVVSAAVSFAPIM SQWWRVGADAEAQRCHSNPRCCAFASNMPYVLLSSSVSFYLPLLVMLFVYARVFVVA TRQLRLLRGELGRFPPEESPPAPSRSLAPAPVGTCAPPEGVPACGRRPARLLPLREHRALC TLGLIMGTFTLCWLPFFLANVLRALGGPSLVPGPAFLALNWLGYANSAFNPLIYCRSPDF RSAFRRLLCRCAAARGRTPPSLGPQDESCTTASSSLAKDTSS (Seq. ID No. 64)

### F. Amino acid sequence of the Edg1R-V2R chimera

MGPTSVPLVKAHRSSVSDYVNYDIIVRHYNYTGKLNISADKENSIKLTSVVFILICCFIILE NIFVLLTIWKTKKFHRPMYYFIGNLALSDLLAGVAYTANLLLSGATTYKLTPAQWFLRE GSMFVALSASVFSLLAIAIERYITMLKMKLHNGSNNFRLFLLISACWVISLILGGLPIMGW NCISALSSCSTVLPLYHKHYILFCTTVFTLLLLSIVILYCRIYSLVRTRSRRLTFRKNISKAS RSSEKSLALLKTVIIVLSVFIACWAPLFILLLLDVGCKVKTCDILFRAEYFLVLAVLNSGT NPIIYTLTNKEMRRAFIRIMSCCKCAAARGRTPPSLGPQDESCTTASSSLAKDTSS (Seq. ID No. 65)